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**Methods:** A study was conducted on 400 9-year-old children from areas with high, optimal and low levels of fluoride in the drinking water of Fars province, Iran. Fluorosis cases were diagnosed on the standardized one view photographs of the anterior teeth using Dean's and TF Indices by calibrated dentists. Agreements between examiners were tested. Early childhood health-related data collected retrospectively by ECEL method were matched with the position of enamel defects.

**Results:** Using both Dean and TF indices three out of four dentists diagnosed that 31.3% (115) children had fluorosis. After matching health-related events in the 115 (31.3%) of children diagnosed with fluorosis, 31 (8.4%) of children had fluorosis which could be matched with their adverse health-related events. That suggests that what was diagnosed as fluorosis were DDEs which may resemble fluorosis.

**Discussion:** The frequently used measures of fluorosis appear to overscore fluorosis. Use of ECEL method to consider health related events relevant to DDEs could help to differentiate between genuine fluorosis and fluorosis-resembling defects.

# **Distinguishing between enamel fluorosis and other enamel defects in permanent teeth of children**

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# Abstract

**Background:** The inconsistent prevalence of fluorosis for a given level of fluoride in drinking water suggests developmental defects of enamel (DDEs) other than fluorosis were being misdiagnosed as fluorosis. The imprecise definition and subjective perception of fluorosis indices could result in misdiagnosis of dental fluorosis. This study was conducted to distinguish genuine fluorosis from fluorosis-resembling defects that could have adverse health-related events as a cause using Early Childhood Events Life-grid method (ECEL).

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**Discussion:** The frequently used measures of fluorosis appear to overscore fluorosis. Use of ECEL method to consider health related events relevant to DDEs could help to differentiate between genuine fluorosis and fluorosis-resembling defects.

# Introduction:

Despite the widescale use of well documented indices of dental fluorosis (Dean 1942; Fejerskov 1988), when using them there is inconsistency in the prevalence rates of fluorosis for a given level of fluoride in drinking water. The inconsistency in reporting fluorosis occurs due to subjective perception of fluorosis by examiners. Therefore, there is a strong possibility that other Developmental Defects of Enamel (DDE) rather than excess intake of fluoride are being misdiagnosed as fluorosis (Atar & Körperich 2010).

The two widely used indices of dental fluorosis are Dean's Index (Dean 1934; Dean 1942) and the TF Index (TFI) (Thylstrup & Fejerskov 1978; Fejerskov 1988). None of them clearly distinguish between defects caused by fluorosis and caused by other factors. The differences between some of the diagnostic categories are uncertain, vague, or insensitive. In Dean's Index, each individual is given one score, as a score for the whole mouth, according to the two teeth most affected by fluorosis. Thylstrup and Fejerskov reformulated Dean' Index as the TF Index (TFI). They used both clinical and histological appearance of fluorosis and created a single coded index from 0 (normal) to 9 (Thylstrup & Fejerskov 1978). The TFI was modified and finalized in 1988 (Fejerskov 1988). Still the differentiation between some categories of TFI is not sufficiently precise.

As the main indices for diagnosing dental fluorosis include definitions that are imprecise, it is not surprising that in some studies the reported prevalence of fluorosis was similar despite the levels of fluoride in the drinking water being similar or different. For example, a study in KwaNdebele (Africa) revealed that the prevalence of fluorosis was similar in residents of areas with considerably different levels of fluoride in the water supply (Lewis & Chikte 1995). A study in Andhra Pradesh (India) of four different areas with different levels of fluoride in drinking water (< 0.7, 0.7-1.2, 1.3-4.0, >4 ppm) reported 100% dental fluorosis even in areas with optimum level of fluoride (Sudhir et al. 2009). In Hong Kong, where the fluoride concentration of public water supplies was increased from 0.5 ppm to 0.7 ppm, and then 1 ppm, the prevalence of DDE of maxillary incisors decreased significantly with increases in the fluoride levels; from 92%, to 55%, and then 35% (Wong et al. 2006).

These inconsistent results suggest that DDEs other than fluorosis were being misdiagnosed as fluorosis. Fluorosis and some DDEs are similar in appearance (Small & Murray 1978; Pindborg 1982). Numerous local and systemic risk factors cause DDEs (Small & Murray 1978; Pindborg 1982; Atar & Körperich 2010). Some DDEs may be of genetic origin (Thesleff 2000; Atar & Körperich 2010) or caused by malnutrition or diseases that occurred during early childhood (Pindborg 1982; Atar & Körperich 2010). Using teeth as markers of significant health related events and considering these risk factors could help to distinguish between genuine fluorosis and fluorosis resembling DDEs.

Genuine fluorosis can best be distinguished from other DDEs by relating a DDE to particular life events, such as a significant health related event. Such events can be reasonably recorded using the life-grid method that helps people remember past events more accurately (Blane 1996). The life-grid method has been widely used and been very successful in obtaining the precise timing of past events in both qualitative and quantitative studies (Berney & Blane 1997; Holland et al. 2000; Bell 2005). A specially designed life-grid for early childhood containing developmental milestones and shorter periods of time for the earlier years, is the Early Childhood Events Life-grid method (ECEL) (Golkari 2009).

As there is a need for accurate data of dental fluorosis, the inconsistency of reports on the prevalence of fluorosis suggests that more precise definitions and diagnostic methods are needed for diagnosing dental fluorosis and distinguishing enamel fluorosis from other DDEs. Therefore a study was planned with the objective of distinguishing genuine fluorosis from fluorosis-resembling defects that could have adverse health-related events as a cause, instead of just excess fluoride intake.

## Materials and methods:

This cross-sectional study was performed on 400 9-year-old children of Fars province, Iran. The children were randomly selected from areas of Iran with high, optimal and low levels of fluoride in the drinking water. Fluorosis cases were diagnosed using Dean's Index and TF Index (Dean 1942; Fejerskov 1988) by calibrated dentists. To differentiate between genuine fluorosis and fluorosis resembling defects, early childhood data were collected retrospectively by the ECEL method (Golkari 2009).

Ethical permission was obtained from the Ethical Committee of Shiraz University of Medical Sciences (SUMS) and the Educational Head Office of the Fars Province. A written consent form explaining the objectives and the stages of the study were sent to the parents of the selected children. They were included only if the parents agreed to take part.

The level of fluoride in water of each town of the province was obtained from their primary health care trust. Towns were categorized into one of three fluoride categories; high ( $>2.0$  ppm), optimal ( $0.7-1.0$  ppm) and low fluoride ( $<0.4$  ppm). One town was selected randomly from each category. The selected towns were Gerash with high fluoride ( $2.12-2.85$ ) in water, Sepidan with low fluoride ( $0.24-0.29$ ) in water, and Shiraz including four zones was the city with an optimal range of fluoride ( $0.62-1.22$ ) in water.

Sample size was calculated based on the estimated prevalence of fluorosis in Iran ( $61\%$ ),  $d=6.1\%$  ( $10\%$  expected prevalence),  $\alpha=0.05$ . As a result, a sample size of 246 was needed if a simple randomized sampling was used in all areas. The selection of children in Gerash and Sepidan (with high and low fluoride levels) was done by simple randomized sampling. However, in Shiraz (chosen as area with optimum fluoride level), the simple randomization was not possible as it was a big city. Therefore, a stratified randomization method had to be adopted. It was done using the four different educational zones of the city. The number of required sample in this area was multiplied by 2 ( $k=2$ ) to increase the accuracy in the stratified sampling method that was used. The response rate was suggested to be around  $80\%$ . Therefore, at the end, 100 9-year-old schoolchildren of Gerash, 100 from Sepidan and 200 from Shiraz were selected from lists of students obtained from Educational Head Office of each town.

Children aged from 9 years, 0 month to 9 years and 11 months who returned the signed consent form were included in the study. Children were excluded if they had lived for more than six months from birth to 5 years of age in other towns. Those who had less than 7 permanent incisor teeth, those with orthodontic brackets, overlapping teeth, and large restorations or severe extrinsic stains on their incisors were also excluded.

Intra-oral examinations were carried out to select children conforming to the study criteria. The examinations were performed using a headlight, disposable mirrors and tongue blades with children seated on a chair. Photographs of the dentition of selected children were taken for the diagnosis of dental fluorosis. A one-view photograph was taken of the anterior part of dentition using a digital camera (Nikon D7100, AF-S VR Micro-Nikkor 105mm f/ 2.8 G IF-ED) based on methods described by Wong et al. (2005). Children were asked to close their incisor teeth edge to edge. Cheeks and lips were retracted so that all anterior teeth and some parts of upper and lower gums were visible. The camera was adjusted to 15 degrees above the perpendicular to the central incisors' plane to minimize specula reflection and burn outs (Ellwood et al. 1996). Immediately after taking each photograph, it was assessed to confirm its quality, and was repeated if necessary.

During the fluorosis assessment phase, first, the photographs were randomly ordered to prevent bias induced by the assessors' foreknowledge of the fluoride in the area. Photographs were then assessed by eight calibrated dentists who were blind to the clinical condition and town of residence of the subjects. Four calibrated dentists assessed the photographs based on Dean's Index, and another four used the TF Index (Dean 1942; Fejerskov 1988). All dentists observed the photographs on one computer with identical settings. The diagnosis of fluorosis was confirmed only if three out of four dentists of each group agreed.

The objective of the next stage of study was to obtain data on early childhood adverse events. The parents of all children participating in the study were invited to school for interview. Name and date of birth of each child were double checked with their parents. Parents were interviewed using the ECEL method (Golkari 2009). Information regarding

gestational age (preterm, term, delayed), birth weight, number of births, type of delivery (natural, caesarean or facilitated delivery), trauma to baby during birth, and newborn vitality score was obtained. Questions were asked relating to personal life line, residential status, occupation of parents/guardians, and child activity line which could help parents to remember adverse health-related events. Afterwards, any illnesses the child had suffered were recorded. For each illness the parent was asked about the name or description of illness, age at which the illness started, duration, perception of severity (mild, moderate, or severe), if went to doctor, medication if used, and hospitalization. Information regarding hospitalizations (age, duration, reason, type of anesthesia if used, and name of hospital), and falls and accidents (age, cause, trauma to face or teeth, hospitalization, and breathing status right after accident as an indicator of severity well known by parents) were also obtained.

The timing of childhood adverse health-related conditions was matched with the timing of formation and calcification of each part of permanent incisors (Golkari 2009). If no adverse life condition could be matched to the position of a defect diagnosed as fluorosis, the case was considered as genuine fluorosis. However, if a health-related adverse condition could be matched to an enamel defect diagnosed as fluorosis, the case was considered as fluorosis-resembling defect. Using this method, diagnosed fluorosis defects were divided into genuine fluorosis and fluorosis resembling defects.

SPSS software (version 22) was used for data analysis. Agreements between examiners who assessed fluorosis using Dean's Index and TF Index were tested using Kappa-coefficient. McNemar, and Pearson correlation tests were also used to compare the results reported by each pair of dentists. The prevalence of fluorosis in the three selected areas was compared by one-way ANOVA. The relationship of fluorosis with the level of fluoride in water, and sex was tested using Logistic regression. Childhood adverse health-related conditions were matched to enamel defects diagnosed as fluorosis one by one.



# Results:

The number of 9-year-old children included in the study was 376; 171 (46%) girls and 196 (53 %) boys. The number of included children from Gerash (high F), Shiraz (optimal F) and Sepidan (low F) were 88, 189, and 90 respectively .

Using both Dean and TF indices, three out of four dentists diagnosed that 31.3% (115) of children had fluorosis. The percentage of fluorosis cases in areas with high, optimal, and low range of fluoride in water was 58.0%, 29.1%, and 10.0% respectively ( $p < 0.001$ ). Logistic regression showed that there was a positive relationship between fluorosis and fluoride in the drinking water ( $p < 0.001$ ). There was no relationship between fluorosis and children's sex ( $p = 0.228$ ).

There were significant differences among dentists who scored photographs using Dean's and TF indices. Among the four dentists who assessed photographs according to Dean's Index, the difference in the number of cases diagnosed as fluorosis was statistically different between each two dentists ( $p < 0.001$ ). There was only a slight (kappa was between 0 and 0.2) or fair (kappa was between 0.2 and 0.4) agreement between them (Table 1). Similar results of agreement were observed among the four dentists who scored children using the TF Index. Although there was not a high agreement among dentists, a positive correlation was observed ( $p < 0.001$ ) (Table 2).

Adverse health-related events were found in 84.7% (311) of children of whom 8.4% of children had fluorosis-resembling defects. After matching health-related events in the 115 (31.3%) of children diagnosed with fluorosis, 31 (8.4%) of children had fluorosis which could be matched with their adverse health-related events. That suggests that what was diagnosed as fluorosis were DDEs which may resemble fluorosis. Therefore, it was concluded that the percentage with genuine fluorosis was 22.9% and not 31.3%. The fluorosis resembling defects (8.4% of all children) included 26.9% of what was diagnosed as fluorosis by Dean's and TF Indices. The percentage of genuine fluorosis in areas with high, optimal and low levels of fluoride in water was 47.7%, 20.6%, and

3.3% respectively. The percentage of fluorosis-resembling defects in areas with high, optimal, and low range of fluoride in water was 10.2%, 8.5%, 6.7% respectively.

## Discussion:

Fluoride is one of the most successful measures for prevention of dental caries in public health (Petersen & Lennon 2004). However, there has always been controversy about using fluoride because of fluorosis (Sapolsky 1968; Null & Feldman 2003; Ananian et al. 2005). Reports of a high prevalence of fluorosis in communities have led to objections to fluoride. Therefore, there is a need for a precise way to diagnose dental fluorosis. Many local and systemic risk factors cause DDEs. Some DDEs are similar to enamel fluorosis and should be differentiated from genuine fluorosis. The difference has not yet been evaluated. The main objective of this study was to distinguish fluorosis that resembled DDEs caused by adverse health-related events, and not caused by excess fluoride intake.

A systematic review reported that the prevalence of fluorosis in Iran was 61%. Considering the average concentration of fluoride in water in Iran was  $0.43 \pm 0.17$  (Azami-Aghdash et al. 2013), the reported prevalence of fluorosis was high and questionable. The inconsistency of the prevalence of fluorosis with the level of fluoride in water reported in that study and in many other different parts of the world (Lo & Bagramian 1996; Sudhir et al. 2009; Arif et al. 2013) suggests that dental fluorosis was misdiagnosed.

The overall prevalence of diagnosed dental fluorosis in the current study was 31.3%. However, by using the ECEL method and considering health-related events, the prevalence of genuine dental fluorosis was 22.6% as there were 8.4% with fluorosis resembling defects. That illustrates that fluorosis could be ruled out as the main cause of about 27% of what was incorrectly diagnosed as fluorosis.

The current study also showed significant differences among the dentists who scored photographs to diagnose fluorosis according to Dean's and TF Indices ( $p < 0.001$ ). This finding indicates that both Dean and TF Indices are too subjective and therefore not precise ways to diagnose dental fluorosis.

These two Indices could lead to misdiagnosis of fluorosis resembling defects as genuine fluorosis. Tavener et al also concluded that interpretation of criteria could be different among examiners and stressed the necessity for standard methods to measure dental fluorosis (Tavener et al. 2007). Some studies have shown good to excellent agreement among examiners (Kumar et al. 2000). However, comparing the methods, the lack of bias was an advantage of the current study, as photographs were assessed instead of clinical examinations.

This study indicates that by considering adverse health-related events, it is possible to distinguish genuine fluorosis from fluorosis-resembling defects. When the timing of an adverse condition matches the timing of development of the part of enamel defect, the adverse event could be the cause of the defect, not fluoride. If no adverse condition could be matched to a defect, excess fluoride could, with caution, be considered as the cause. On the other hand, if fluoride is considered the cause of defects, such defects should not be seen on the teeth of children who experienced the same adverse health-related conditions and were living in areas with low levels of fluoride in water. In case of generalized defects, fluoride, genetic, or severe underlying systematic disease, either individually or as a combination could be the cause.

One limitation of this study is that even if an adverse health-related event could be exactly matched to a fluoride-resembling defect in terms of time and place, it could not be definitely considered that the adverse event was the cause of the defect and fluoride was not the cause. On the other hand, if an adverse condition could not be matched to a supposedly fluorosis defect, one could not be sure that fluoride was the cause. In fact, the definite diagnosis of fluorosis is not possible by this method and the only exact way to diagnose dental fluorosis would be by microscopic or chemical analysis. However,

although the ECEL method cannot prove that fluoride is or is not the cause of defect, it can help in differentiate between genuine fluorosis and fluorosis-resembling defects.

The diagnosis of fluorosis is more complicated than acknowledged. Existing fluorosis indices could lead to misjudgment about using fluoride. However, the ECEL method to record health-related life events is a promising method to help differentiate between genuine fluorosis and fluorosis-resembling defects.

## Conclusion:

Fluorosis indices, if used alone, could result in misdiagnosis of dental fluorosis. Information about adverse health-related conditions linked to DDEs at specific positions on teeth could help to differentiate between genuine fluorosis and fluorosis-resembling defects.

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335 Table1. The comparison of fluorosis scores according to Dean's Index by four calibrated  
336 dentists

	Test	Examiner 2	Examiner 3	Examiner 4
Examiner 1	Kappa value	0.16	0.16	0.07
	McNemar p-value	<0.001	<0.001	<0.001
	Correlation coefficient	0.528	0.454	0.458
Examiner 2	Kappa value		0.34	0.37
	McNemar p-value		0.125	<0.001
	Correlation coefficient		0.584	0.575
Examiner 3	Kappa value			0.29
	McNemar p-value			0.003
	Correlation coefficient			0.614

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339 Table 2.The comparison of fluorosis scores according to TF Index by four calibrated  
340 dentists

	Test	Examiner 2	Examiner 3	Examiner 4
Examiner 1	Kappa value	0.06	0.21	0.34
	McNemar p-value	<0.001	<0.001	<0.001
	Correlation coefficient	0.381	0.465	0.498
Examiner 2	Kappa value		0.27	0.18
	McNemar p-value		<0.001	<0.001
	Correlation coefficient		0.472	0.503
Examiner 3	Kappa value			0.36
	McNemar p-value			<0.001
	Correlation coefficient			0.539

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